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(FILE 'HOME' ENTERED AT 15:07:18 ON 20 OCT 2010)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, LIFESCI' ENTERED AT 15:07:51 ON  
20 OCT 2010

L1 2221205 S AGITAT? OR STIR? OR ROTAT? OR ROCK?  
L2 6067 S SINGLE(W)CELL(4A)SUSPENSION  
L3 230264 S (PLURIPOTENT OR EMBRYONIC OR ES OR EG) (4A)CELL  
L4 1070 S L1(P)L3  
L5 8193 S EMBRYOID(W)BODY  
L6 140 S L4 AND L5  
L7 8 S L2 AND L6  
L8 32 S L2 AND L4  
L9 2 DUP REM L7 (6 DUPLICATES REMOVED)  
L10 10 DUP REM L8 (22 DUPLICATES REMOVED)

=> d bib ab 1-2 19

L9 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1  
AN 2005625071 MEDLINE  
DN PubMed ID: 16189818  
TI Differentiation and lineage selection of mouse embryonic stem  
cells in a stirred bench scale bioreactor with automated  
process control.  
AU Schroeder Magnus; Niebruegge Sylvia; Werner Andreas; Willbold Elmar; Burg  
Monika; Ruediger Manfred; Field Loren J; Lehmann Juergen; Zweigerdt Robert  
CS Institute of Cell Culture Technology, University of Bielefeld, 33501  
Bielefeld, Germany.  
SO Biotechnology and bioengineering, (2005 Dec 30) Vol. 92, No. 7, pp.  
920-33.  
Journal code: 7502021. ISSN: 0006-3592. L-ISSN: 0006-3592.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200602  
ED Entered STN: 29 Nov 2005  
Last Updated on STN: 3 Feb 2006  
Entered Medline: 3 Feb 2006  
AB It is well established that embryonic stem (ES)  
cells can differentiate into functional cardiomyocytes in vitro.  
ES-derived cardiomyocytes could be used for pharmaceutical and therapeutic  
applications, provided that they can be generated in sufficient quantity  
and with sufficient purity. To enable large-scale culture of ES  
-derived cells, we have developed a robust and scalable  
bioprocess that allows direct embryoid body (EB)  
formation in a fully controlled, stirred 2 L bioreactor  
following inoculation with a single cell  
suspension of mouse ES cells. Utilizing a  
pitched-blade-turbine, parameters for optimal cell expansion as well as  
efficient ES cell differentiation were established.  
Optimization of stirring conditions resulted in the generation  
of high-density suspension cultures containing  $12.5 \times 10^6$  cells/mL after  
9 days of differentiation. Approximately 30%-40% of the EBs formed in  
this process vigorously contracted, indicating robust cardiomyogenic  
induction. An ES cell clone carrying a recombinant  
DNA molecule comprised of the cardiomyocyte-restricted alpha myosin heavy  
chain (alphaMHC) promoter and a neomycin resistance gene was used to  
establish the utility of this bioprocess to efficiently generate  
ES-derived cardiomyocytes. The genetically engineered ES

cells were cultured directly in the stirred bioreactor for 9 days, followed by antibiotic treatment for another 9 days. The protocol resulted in the generation of essentially pure cardiomyocyte cultures, with a total yield of  $1.28 \times 10^9$  cells in a single 2 L bioreactor run. This study thus provides an important step towards the large-scale generation of ES-derived cells for therapeutic and industrial applications.

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L9 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2  
AN 2003500944 MEDLINE  
DN PubMed ID: 14578102  
TI Generation of confluent cardiomyocyte monolayers derived from embryonic stem cells in suspension: a cell source for new therapies and screening strategies.  
AU Zweigerdt R; Burg M; Willbold E; Abts Hf; Ruediger M  
CS Cardion AG, Erkrath, Germany.  
SO Cytotherapy, (2003) Vol. 5, No. 5, pp. 399-413.  
Journal code: 100895309. ISSN: 1465-3249. L-ISSN: 1465-3249.  
CY England: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200401  
ED Entered STN: 28 Oct 2003  
Last Updated on STN: 30 Jan 2004  
Entered Medline: 29 Jan 2004  
AB BACKGROUND: Cellular cardiomyoplasty is evolving as a new strategy to treat cardiac diseases. A prerequisite is a reliable source of pure cardiomyocytes, which could also help in the exploitation of recent advances in genomics and drug screening. Our goal was to establish a robust lab-scale process for the generation of embryonic stem (ES)-cell-derived cardiomyocytes in suspension. METHODS: A 71 ES cell clone carrying a construct consisting of the alpha-cardiac myosin heavy chain (alphaMHC) promoter driving the neomycin resistance gene was used for antibiotic-driven cardiomyocyte enrichment. Rotating suspension culture was established to initiate embryoid body (EB) formation. To track growth and differentiation kinetics, cell count and flow cytometry for SSEA-1, E-cadherin (stem-cell marker) and sarcomeric myosin (cardiomyocytes marker) was performed. Oct4 expression was measured via real time (RT)-PCR. RESULTS: Cultures comprising  $2.5-8 \times 10^6$  differentiating ES cells/mL were obtained after 9 days in rotating suspension. Upon G418 addition, vigorous contracting spheres, termed cardiac bodies (CB), developed. These cultures consisted of about  $2.1 \times 10^5$  enriched cardiomyocytes/mL after 6-10 days of selection. Suspensions comprising 90-95%viable single cells were generated using an improved dissociation method. Seeding of cardiomyocytes with  $7 \times 10^4$  cell/cm<sup>2</sup> resulted in a homogeneous monolayer of synchronously contracting cells. Myocyte specific immunohistochemistry indicated purity of > 99%. DISCUSSION: We have established a reliable lab-scale protocol to generate cultures of highly enriched cardiomyocytes in suspension. This will facilitate development of larger-scale processes for stem-cell based cardiomyocyte supply. An improved method is provided to derive vital suspensions of cardiomyocytes, which could be utilized for transplantation as well as for drug screening purposes.

=> d au ti so pi l-10 110

L10 ANSWER 1 OF 10 MEDLINE on STN

DUPLICATE 1

- AU Mason Mariah N; Mahoney Melissa J  
TI Inhibition of gamma-secretase activity promotes differentiation of embryonic pancreatic precursor cells into functional islet-like clusters in poly(ethylene glycol) hydrogel culture.  
SO Tissue engineering. Part A, (2010 Aug) Vol. 16, No. 8, pp. 2593-603.  
Journal code: 101466659. E-ISSN: 1937-335X. L-ISSN: 1937-3341.  
Report No.: NLM-PMC2947432 [Available on 08/01/11].
- L10 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 2  
AU Schmidt-Ott Kai M  
TI ROCK inhibition facilitates tissue reconstitution from embryonic kidney cell suspensions.  
SO Kidney international, (2010 Mar) Vol. 77, No. 5, pp. 387-9.  
Journal code: 0323470. E-ISSN: 1523-1755. L-ISSN: 0085-2538.
- L10 ANSWER 3 OF 10 LIFESCI COPYRIGHT 2010 CSA on STN DUPLICATE 2  
AU Olimer, R.; Haase, A.; Merkert, S.; Schwanke, K.; Cui, W.; Martin, U.  
TI Expansion of undifferentiated human iPS and human ES cells in suspension culture using a largely defined medium  
SO Human Gene Therapy [Hum. Gene Ther.], (20091100) vol. 20, no. 11, p. 1394.  
ISSN: 1043-0342.
- L10 ANSWER 4 OF 10 MEDLINE on STN DUPLICATE 3  
AU Vereyken E J F; Fluitsma D M; Bolijn M J; Dijkstra C D; Teunissen C E  
TI An in vitro model for de- and remyelination using lysophosphatidyl choline in rodent whole brain spheroid cultures.  
SO Glia, (2009 Sep) Vol. 57, No. 12, pp. 1326-40.  
Journal code: 8806785. E-ISSN: 1098-1136. L-ISSN: 0894-1491.
- L10 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 4  
AU Li Xiangyun; Krawetz Roman; Liu Shiyi; Meng Guoliang; Rancourt Derrick E  
TI ROCK inhibitor improves survival of cryopreserved serum/feeder-free single human embryonic stem cells.  
SO Human reproduction (Oxford, England), (2009 Mar) Vol. 24, No. 3, pp. 580-9. Electronic Publication: 2008-12-04.  
Journal code: 8701199. E-ISSN: 1460-2350. L-ISSN: 0268-1161.
- L10 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 5  
AU Schroeder Magnus; Niebruegge Sylvia; Werner Andreas; Willbold Elmar; Burg Monika; Ruediger Manfred; Field Loren J; Lehmann Juergen; Zweigerdt Robert  
TI Differentiation and lineage selection of mouse embryonic stem cells in a stirred bench scale bioreactor with automated process control.  
SO Biotechnology and bioengineering, (2005 Dec 30) Vol. 92, No. 7, pp. 920-33.  
Journal code: 7502021. ISSN: 0006-3592. L-ISSN: 0006-3592.
- L10 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN  
AU Schroeder, M.; Niebruegge, S.; Werner, A.; Zweigerdt, R.; Burg, M.; Lehmann, J.  
TI Optimizing the production of cardiomyocytes from mouse embryonic stem cells in a 2L stirred tank reactor  
SO Animal Cell Technology Meets Genomics, Proceedings of the ESACT Meeting, 18th, Granada, Spain, May 11-14, 2003 (2005), Meeting Date 2003, 285-288.  
Editor(s): Godia, Francesc; Fussenegger, Martin. Publisher: Springer, Dordrecht, Neth.  
CODEN: 69HJAV; ISBN: 1-4020-2791-5
- L10 ANSWER 8 OF 10 MEDLINE on STN DUPLICATE 6  
AU Zweigerdt R; Burg M; Willbold E; Abts Hf; Ruediger M  
TI Generation of confluent cardiomyocyte monolayers derived from embryonic

- stem cells in suspension: a cell source for new therapies and screening strategies.
- SO Cytotherapy, (2003) Vol. 5, No. 5, pp. 399-413.  
Journal code: 100895309. ISSN: 1465-3249. L-ISSN: 1465-3249.
- L10 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 7  
AU Ihara S; Watanabe M; Nagao E; Shioya N  
TI Formation of hair follicles from a single-cell  
suspension of embryonic rat skin by a two-step procedure *in vitro*.  
SO Cell and tissue research, (1991 Oct) Vol. 266, No. 1, pp. 65-73.  
Journal code: 0417625. ISSN: 0302-766X. L-ISSN: 0302-766X.
- L10 ANSWER 10 OF 10 MEDLINE on STN DUPLICATE 8  
AU Hausman R E; Berggrun D A  
TI Prostaglandin binding does not require direct cell-cell contact during  
chick myogenesis *in vitro*.  
SO Experimental cell research, (1987 Feb) Vol. 168, No. 2, pp. 457-62.  
Journal code: 0373226. ISSN: 0014-4827. L-ISSN: 0014-4827.

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